International Journal of Educational
Science and Research (IJESR)
ISSN (P): 2249–6947; ISSN (E): 2249–8052
Vol. 11, Issue 2, Dec 2021, 173–178

AMBERLITE IR-120 RESIN CATALYSED N-TERT-BUTYLOXY CARBONYLATION OF AMINES UNDER THE SOLVENT-FREE CONDITIONS

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ABSTRACT

An effective and green procedure for N-tert-butyloxy carbonylation of amines using Amberlite IR-120 resin under solvent-free conditions was reported. Several amines were protected by using this methodology. This methodology has advantages of mild conditions, rapid reaction, excellent yield, solvent-free, and green synthesis.

KEYWORDS: Amberlite IR-120 Resin; Amines; N-Tert-Buty loxy carbonylation; Green Synthesis & Solvent-Free

Received: Sep 07, 2021; **Accepted**: Sep 27, 2021; **Published**: Dec 08, 2021; **Paper Id**.: IJESRDEC202119

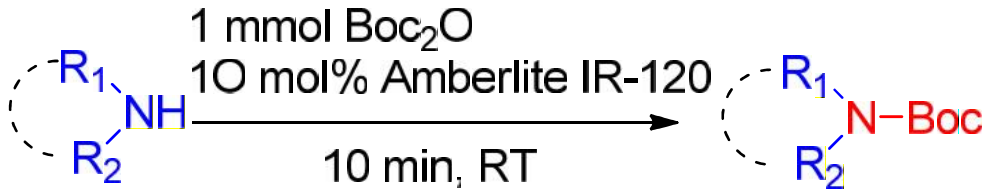
Original Article

INTRODUCTION

Choosing the correct protecting group in organic synthesis is challenging.[1] Several bioactive compounds, drugs, natural products are rich sources of amino group that plays an important role in many biological functions. Protection of amino group as well as its deprotection play's important role in organic reactions.[2] Several reagents were used to protect the amino group in the organic reactions. In these protection groups, tert-butyloxy carbonylation (N-Boc) protection becomes extensively used approach in synthetic organic chemistry. [3]Since this group is easily removed using CF_3COOH, or thermolys is and stable under basic and inert conditions.[4] Therefore N-Boc protection of amines was widely used in amines, amino acid, and peptide synthesis.

Different strategies were used in the literature to protect amines with Boc anhydride using various base catalysts, Lewis or Bronsted acid catalysts, heterogeneous catalysts, and ionic liquids. [5-10] Most of the methods have advantages in some cases, but they have some disadvantages, such as keepingdry conditions, less yields, limited functional group tolerance, slow reaction rate and purification. Thus, there is a requirement of an environmentally benign, simple, rapid and solvent-free protocol for N-Boc protection using a recyclable catalyst is required.

The use of nontoxic catalyst and solvent free protocols become an important role in the development of organic molecules. Usage of acidic resin catalyst such as Amberlite IR-120 resin hasbecomeas eco-friendly, heterogeneous and cost-effective catalyst. Amberlite IR-120 resin shows advantages such as high catalytic activity, recyclability, easy handling, and less toxicity.[11-18]Herein, we report a greener protocol for N-Boc protection of various functionalized amines at room temperature in excellent yields. **(Scheme 1)**



Scheme 1: N-Boc protection using Amberlite IR-120 resin

RESULT AND DISCUSSIONS

To examine the feasibility of this reaction, we selected aniline **(1a)** as a model substrate. Aniline was treated with Boc_2O using amberlite IR-120 resin under the solvent-free conditions at RT (Table 1). The reaction was slow when there is no catalyst after 8 h to get N-Boc aniline **(2a)** (Table 1, entry 1).To check the usage of the selected catalyst and improve the yield, the reaction was done using 5 mol.% of Amberlite IR-120 resin under similar conditions. Remarkably, there is a significant improvement in the yield of N-Boc protected aniline **(2a)** was observed and the yield was increased to 82% within 20 min (Table 1, entry 2). Now we want to check and optimize the amount of catalyst. For this, a model reaction was carried out using different mole percentage of catalyst. After several experiments, usage of 10 mo l.% of Amberlite IR-120 resin increased the product yield from 82% to 98% within 10 minutes (Table 1, entries 3). Increase in the catalyst from 10 to 15 mol% of catalyst produced the same yield of the product within 10 minutes for getting N-Boc aniline**2a** (Table 1, entry 4).

Further, we screened the recyclability of Amberlite IR-120 resin and reused for 5 trials. There is no significant change in the yield of product was observed after the reuse of catalyst several times. After the reaction, MTBE was added and the catalyst was removed by filtration. The catalyst was dried and used without any purification. The catalyst showed that Amberlite IR-120 resin was maintained its catalytic activity after 5 times. Compound **2a** was attained in 98%, 98%, 97%, 96% and 95% yields respectively after the successive five efficient rounds (Table 1, entry 5).

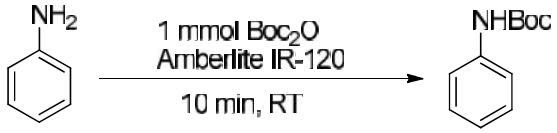


Table 1: Optimization of mol% of Catalyst for the Preparation of N-Boc aniline.

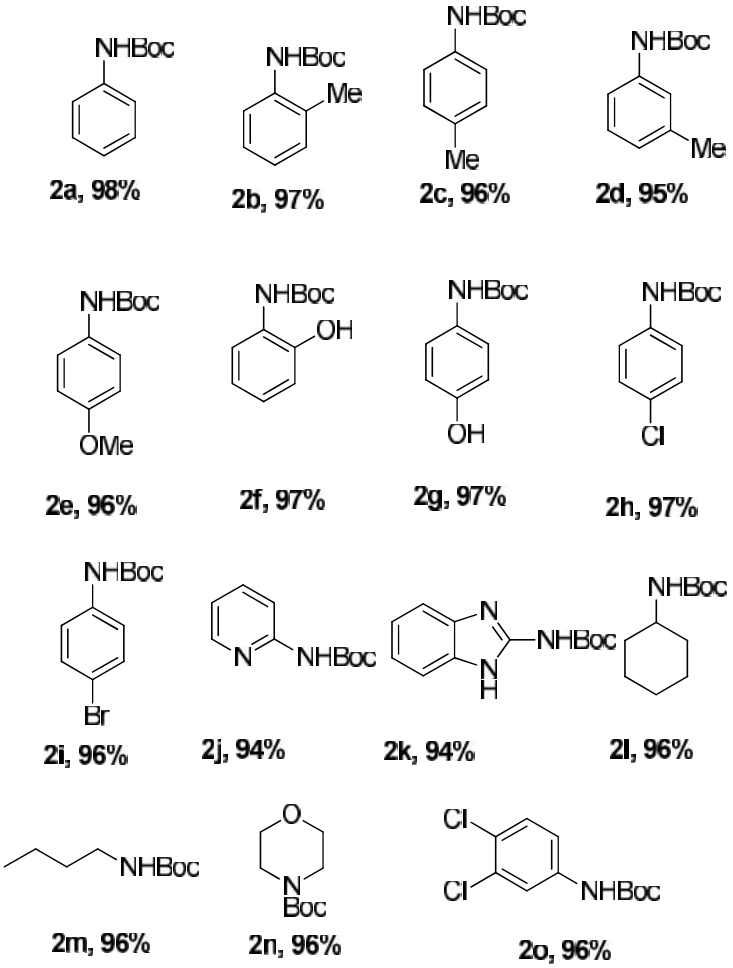
Entry[a]	Catalyst (mol%)	Time (min)	Yield[b] (%)
1	-	480	40
2	5	20	82
3	10	10	98
4	15	10	98
5[c]	10	10	98,98,97,96,95

A Reaction conditions: 1a (1 mmol), Boc2O (1 mmol) were stirred in presence of 10 mol.% of catalyst at room temperature.
bYield of isolated product.
cCatalyst was reused five times.

To explore the scope and generality of Amberlite IR-120 resin mediated N-Boc protection of amines, different

functionalized amines were used under improved conditions. The results were presented in Table 2. The protocol was tested for N-Boc protection of different amines. In general aniline and aryl amines containing electron donating groups undergoes the N-Boc protection in less reaction time with good yields. The halogens substituted anilines were also undergone the N-tert-butyloxy carbonylation under the optimized reaction condition in good to moderate yield (Table 2). Though, the reaction was slow at RT for the anilines containing electron withdrawing groups. Other aromatic amines were underwent to form the respective N-Boc derivatives in exceptional yields in 10–15 min (Table 2). All the synthesized compounds were confirmed by their analytical data.

Table 2: N-Boc Protection of Aromatic Amines by Amberlite IR-120 Resin



CONCLUSIONS

Amberlite IR-120 resin is a green, efficient, recyclable, eco-friendly catalyst for the N-Boc protection of verity of functionalized amines in good to excellent yields in less reaction time. The process is having advantages such as 1) rapid reaction rate, 2) mild conditions, 3) good functional group tolerance, 4) excellent yield, 5) solvent-free, and 6) excellent catalyst recyclability.

Experimental Section

Synthesis Procedure for N-Boc Protection of Amines

A mixture of amine (1 mmol.) and Boc_2O (1 mmol), 10 mol% Amberlite IR-120 resin were stirred at room temperature. After the completion MTBE was added and the catalyst was removed by simple filtration. After solvent evaporation, the pure products were obtained without any further purification.

Tert-butyl (3,4-dichlorophenyl)carbamate (2o)

White color solid; m.p. 102–103 ^{0}C; Yield 94%; ^{1}H NMR (500 MHz, $CDCl_3$):δ 7.64 (s, 1H), 7.31 (d, J=8.9 Hz, 1H), 7.14 (d, J=8.7 Hz, 1H), 6.72 (br s, 1H), 1.52 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.4, 137.9, 132.6, 130.3, 126.0, 120.1, 117.7, 81.2, 28.2;HRMS calc. for $C_{11}H_{13}C_{l2}NO_2Na$ (M+Na)+ 284.0221 found 284.0230.

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